

Clinical Aspects of High-Altitude Illness

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Abstract

High-altitude illness includes acute mountain sickness (AMS), high-altitude cerebral edema (HACE) and high-altitude pulmonary edema (HAPE). Taiwan is a mountainous island and the high-altitude illness is relatively common. Actually, 28% of Jade mountain (3,952 m) climbers met the diagnoses of AMS. This article reviews recent update of pathophysiology of high-altitude illness and provides evidence in the management of high-altitude illness. (*Ann Disaster Med.* 2004;2 Suppl 2: S53-S60)

Key words: High-Altitude Illness; Acute Mountain Sickness; High-Altitude Cerebral Edema; High-Altitude Pulmonary Edema

Introduction

Taiwan lies off the southeastern coast of mainland Asia, across the Taiwan straits from mainland China, with total land area about 36,000 square kilometers. In this tiny area, there are 293 mountains over 3000 meters. Rapid ascending is possible through convenient road traffic from adjacent plain region. During high season for climbing and ski, it was assumed the prevalence of high-altitude illness should be high among travelers and inexperienced climbers. However, because vague symptoms of early acute mountain sickness (AMS) were easily recognized as common cold, the true incidence remained unknown until 2002, a survey conducted by Kuo et al. revealed 28% of Jade mountain (3,952 m) climbers met the diagnoses of AMS.¹ There was no available data on the incidence of high-altitude cerebral edema

(HACE) and high-altitude pulmonary edema (HAPE) in Taiwan. However, it was speculated that these two unusual and unaware illnesses may be potential causes of high mountain emergencies in past decades in Taiwan Alps region. This article provides pathophysiological updates and contemporary treatments consensus of high-mountain illness.

Acute Mountain Sickness (AMS)

The initial symptoms of AMS can be subtle and misleading, including dizziness, weakness, difficulty sleeping, nausea, and vomiting. Sometimes these symptoms may be confused with hangover, viral illness or CO poisoning caused by using stove in tents. Based on the consensus of 1991 International Hypoxia Symposium at Lake Louise, Canada,² the clinical diagnosis of

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AMS was made in the setting of recent ascend combined with 2 associated symptoms (Table).

Well recognized risk factors of high-altitude diseases including ascending rate, attained altitude, sleeping altitude, and personal susceptibility. Women are more susceptible than men. Different locations have incidences variant with accessibility and altitude. Physical fitness is not protective against AMS, but can increase exercise tolerance and contribute to maintain activity under the influence of AMS. Person with previous history of AMS will encounter similar symptoms on repeat exposures. This phenomenon also suggests that genetic variance may be related with AMS susceptibility. The other personal factors found

related with AMS including low hypoxic ventilatory response and low vital capacity.

The hallmark of AMS is brain swelling caused by brain vasodilatation with impaired autoregulation. Although hypoxia-induced vasodilatation is the obvious cause in the setting of high altitude, hypobaria can be a contributive factor as one study found that AMS are worse with the combination of normal oxygen and hypobaria than with hypoxia and normal pressure.³ Vasogenic edema was proved by neuroimaging in patients of moderate to severe AMS.⁴ The leaky blood-brain barrier is the consequence of impaired autoregulation and the hypoxia insult. Hypoxia induced mediators, eg. Vascular endothelial growth factor (VEGF),

Table. Consensus of 1991 International Hypoxia Symposium at Lake Louise, Canada

AMS	In the setting of a recent gain in altitude, the presence of headache and at least one of the following symptoms: <ul style="list-style-type: none"> - gastrointestinal (anorexia, nausea or vomiting) - fatigue or weakness - dizziness or lightheadedness - difficulty sleeping
HACE	Can be considered "end stage" or severe AMS. In the setting of a recent gain in altitude, either: <ul style="list-style-type: none"> - the presence of a change in mental status and/or ataxia in a person with AMS - or, the presence of both mental status changes and ataxia in a person without AMS
HAPE	In the setting of a recent gain in altitude, the presence of the following: Symptoms: at least two of: <ul style="list-style-type: none"> - dyspnea at rest - cough - weakness or decreased exercise performance - chest tightness or congestion Signs: at least two of: <ul style="list-style-type: none"> - crackles or wheezing in at least one lung field - central cyanosis - tachypnea - tachycardia

NO synthase and bradykinin were all associated with increased blood-brain barrier permeability.⁵

Current treatment of AMS consists of stopping the ascent, descending to lower altitude or acclimatizing at same altitude. However, vigorous exercise should be avoided during descent. Medications for AMS include acetazolamide (Diamox) 250 mg PO tid,⁶ analgesics (aspirin 650 mg, acetaminophen 650-1000 mg, or ibuprofen 600-800 mg) and antiemetics (Prochlorperazine 5 -10 mg IM/PO q6-8h).

There are 3 principles for moderate AMS: descent, O₂, and steroid. If symptoms are worsening, immediate descent or using portable hyperbaric devices (Gamow bag or Chamberlite bag) should be considered. These devices can simulate 2000 m descent after pressurized to 2 psi (13.8 kPa). Low flow O₂ (0.5 – 1.0 L/min) effectively relieves symptoms but is usually not available. Dexamethasone can be given 4 mg PO/IV/IM q6h. Usually, IV or IM route is preferred because of severe vomiting. Adverse effects of acetazolamide include polyuria, paraesthesia, and taste disturbance. Dexamethasone may cause depression, hyperglycemia and potential rebound symptoms if taper period is omitted.

Prevention of AMS can be achieved by gradual ascent (< 500 m/day) for acclimatization without aids of medication⁷. However, if rapid ascent is expected, Acetazolamide 250 mg PO tid should be started 24 h before ascent and continued for the first 2 days. Small doses of acetazolamide have been proposed (125 mg PO bid) with controversy. For those allergic to sulfa drugs, dexamethasone 4 mg PO q12h starting the day of ascent and continuing for the first 2 days is an alternative⁸. Ginkgo

biloba reduces AMS symptoms during rapid ascent in several non-randomized studies,^{9,10} However, in 2004, Gertsch et al. published a double blind, randomized control trial found ginkgo is not effective in decreasing the incidence or severity of AMS, and the efficacy of acetazolamide for preventing headache was even decreased when combined with ginkgo.

Current suggestion for graded ascent is to rest one night at 1500 to 2000 m before any sleep altitude over 2500 m. Starting at 3000 m, climbers should spend 2 nights for 1000 m gain in sleeping altitude. Proper climbing plan can offer better ascent strategy and also help to avoid overexertion, alcohol, sedative drugs and high-carbohydrate diet.

High-Altitude Cerebral Edema (HACE)

High-altitude cerebral edema is diagnosed clinically² once AMS patients have ataxia or mental status change. The ataxia can be examined by 6-steps tandem gait test. However, finger-nose-finger test was not affected by HACE and focal neurologic signs are rare.

HACE is the end stage of AMS, representing physiologic compensate mechanism had been failed. Hence, the reasonable action is either immediate descent or emergent evacuation. Similar treatments for AMS can be administered while during descent or waiting for rescue. Portable hyperbaric device can be life-saving if descent is temporarily impossible. O₂ 2-4 L/min for keeping SaO₂ > 90%, dexamethasone 8 mg PO/IM/IV, then 4 mg q6h, and Acetazolamide should be started. Left untreated, the patient may become stupor, comatose, and eventually die from brain herniation. The coma stage may prolonged for weeks even after evacuation, however, the

prognosis is good with rare permanent sequelae.

High-Altitude Pulmonary Edema (HAPE)

HAPE accounts for most fatalities from high altitude illnesses. It occurs to 5 to 10% of AMS patients. Risk factors are similar to those of AMS: rapid ascent, cold, overexertion, reached altitude, and personal susceptibility. Men have higher incidence than women. It is also more common in persons under 20 years of age. Pulmonary hypertension of any cause increases risk for development of HAPE. Therefore, any patient has recurrent HAPE or HAPE at altitude below 2500 m should be evaluated for possible intracardiac shunts (atrial septal defect, patent ductus arteriosus, patent foramen ovale), drug-induced pulmonary hypertension (phentermine), chronic pulmonary embolism, mitral valve stenosis or idiopathic pulmonary hypertension.¹²

Most frequent early symptoms of HAPE are dry cough and decreased exercise performance. Foamy sputum and respiratory distress are seen in the late stage. Mild fever is common, and should not be easily recognized as a sign of pneumonia. Crackles are first auscultated in the right axilla and will spread bilaterally later. The Lake Louise criteria (Table 1) required at least 2 symptoms and 2 signs presented in the setting of recent ascent. Although the assessment of initial crackles may be difficult to inexperienced climbers, the resting tachypnea and tachycardia can be easily appreciated even without training. Because of the high mortality of unrecognized HAPE, therapeutic measures should be taken even when diagnosis was in doubt.

Contrary to HACE, the underlying pathophysiology of HAPE is exaggerating hypoxic pulmonary vasoconstriction.¹³ Elevated pulmonary artery pressure (PAP) causes regional capillary overperfusion and subsequent leakage by stress failure. This theory explained the heterogeneous pattern of chest radiography of HAPE sufferer.

The decreased capacity for the active reabsorption of alveolar fluid was suspected as another possible answer of HAPE by the experiment on gene-transfected animal model.¹⁴ ¹⁵ Amiloride-sensitive sodium channels (ENaC) in the alveolar epithelial cells help to remove the excess alveolar infiltrates by Na⁺ reabsorption. Knowles et al.¹⁶ use nasal epithelial potential difference as a surrogate measurement to evaluate ion transport activity in airway epithelia and find HAPE-sensitive climbers have significant lower potential difference than control. However, in the recent study by Mairbaurl et al,¹⁷ the amiloride-sensitive nasal epithelial difference potential (NP_{Δamil}) was shown to be inversely related with Cl⁻ secretion, which substantially increased for compensating drying of the nasal mucosa at high altitude. There is no difference of NP_{Δamil} between HAPE-sensitive and control group whether at low or high altitude. As a result, the channel-defect theory cannot be proven at alveolar level at present.

Treatments for HAPE are immediate descent, O₂, and nifedipine. Overexertion during descent was related to increased mortality and should be avoided at all cost. Oxygen readily reduces pulmonary artery pressure 30 to 50 percent. Supplemental O₂ should be titrated to keep SpO₂ > 90%, otherwise, immediate descent is necessary. Nifedipine 10 mg

PO q4-6h or 30 mg extended release q12h reduce pulmonary artery pressure but barely increase the arterial oxygen partial pressure. It should be preserved as the last measure when descent is impossible and O₂ is unavailable. Nitric oxide is effective for HAPE,¹⁸ Since NO and oxygen have equal accessibility, there is no evidence suggest use NO instead of O₂. Mask for providing positive end-expiration pressure helps to enhance arterial oxygen partial pressure and can be used temporarily if available.

Salmeterol 125 μ g inhalation twice a day (Serevent, Glaxowellcome) was shown to be effective in prevention of HAPE.¹⁹ It was suggested Salmeterol works through stimulation of sodium reabsorption. However, other mechanisms as tightening of the alveolar-capillary barrier, lowering pulmonary-artery pressure directly and through mediation by peripheral chemoreceptors, as well as indirectly through hypoxic ventilatory stimulation and increased nitric oxide production were proposed by Bärtsch et al.²⁰

Other High-Altitude Threats

High-altitude pharyngitis and bronchitis are common in people who stayed over two weeks at altitudes above 5500 m. Dehydration, high ventilation and dry cold air are causes of the pharyngitis and bronchitis. Steam inhalation, face mask, hard candies and force hydration are helpful. However, because symptoms of bronchitis are similar to early HAPE, climbers should be alert to any signs of decreased exercise performance.

Pulmonary embolism, stroke and deep venous thrombosis are more likely to occur at high altitude because of dehydration and polycythemia. Once these complications

occurred, patients should be evacuated to lower altitude and admitted.

Peripheral edema is common at high altitude, and can be treated by diuretics. Usually it will resolve spontaneously even without specific treatment. Concurrent HAPE or HACE is possible because of the overloaded volume status and should not be overlooked.

High-altitude retinopathy is related to hypoxia. Fundoscope examination reveals tortuosity and dilation of retinal veins, disk hyperemia, retinal edema and retinal hemorrhage. Retinal hemorrhages are asymptomatic and usually resolve after one to two weeks. Descent is recommended only if macular hemorrhage occurs with visual impairment (scotomata).

Ultraviolet keratitis is also known as snow blindness. Thinner and cleaner atmosphere at high altitude absorb less UV light, and the rock or snow reflection make the situation even worse. Cornea can be easily burned by UVB in one hour, but symptoms usually develop after six to twelve hours. Foreign body sensation, photophobia, tearing, chemosis and conjunctival erythema are typical presentation. Cold compression, eye patches, and oral analgesics are necessary for comfort. The keratitis usually resolves spontaneously in 24 hours. Sun glasses or polarizing lenses are useful preventions.

Summary

The simplest way to deal with high-altitude diseases is prevention. There is no enough evidence to persuade patients with history of acute mountain sickness out of climbing. However, because there is no definite way to predict the personal susceptibility of HAPE/HACE, the current best policy is to counsel patients with

episodes of HAPE or HACE not to reach the same altitude without proper equipment (O₂ or portable hyperbaric device) and adequate acclimatization. For those mountaineers have never been to the altitude over 3000 m, it is wise to undergo similar-altitude training at medical-equipped base first and make the scheduled climbing by graded ascent. At any circumstance, descent is always the best answer for high-altitude illness if possible.

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高山症

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摘要

高山症包括急性高山病，高山腦水腫以及高山肺水腫。台灣是個多山的島嶼，高山症相對常見。實際上高達28% 攀登玉山 (3,952 公尺) 的山友符合急性高山病的診斷。本文回顧最近關於高山症候群的病理生理學研究，並提供高山症處置的醫學證據。(Ann Disaster Med. 2004;2 Suppl 2:S53-S60)

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